Human Gene Therapy for Rare Diseases (Draft Guidance for Industry)

SciPol Summary

The Food and Drug Administration (FDA) released a guidance document, Human Gene Therapy for Rare Diseases, in July 2018. This document intends to provide recommendations to help stakeholders develop studies to develop products for treating rare diseases that are limited by population size, which can prevent an accurate assessment of the safety and efficacy of the developed product. As of July 2018, most rare diseases, which collectively affect 25 million Americans, have no approved therapies, representing an unmet need for new and effective treatments. Despite stakeholders seeking opportunities to develop therapies, there are many obstacles preventing drug development; these hurdles include that a single disease can arise from multiple mutations, there are often diverse clinical manifestations, and often there are varying rates of disease progression.

This guidance seeks to address these obstacles through recommendations in three broad categories:

1. Considerations for product development.

The guidance emphasizes that it is difficult to develop gene therapies (GT) for rare diseases due to the limited population size affected by any one of these diseases. Typically, large trial populations allow for the characterization of the drug to ensure its safety and efficacy. Thus, for rare disease GT products, the FDA highlights the need for well-controlled manufacturing processes and appropriate analytical assays prior to clinical trials. The FDA further recommends that stakeholders contact the Office of Tissues and Advanced therapies (OTAT) for product-specific recommendations. The OTAT will provide guidance on how to interpret treatment effects, design studies to assess product standards, and recommendations regarding how to scale-up production.

2. Considerations for preclinical studies.

Preclinical trials are performed to identify appropriate dosage schedules, establish the route of administration, identify potential toxicities, and determine subject eligibility criteria. As an example, the FDA recommends using proof-of-concept studies to measure biological responses to the GT product and ensure that these responses are similar to the expected human response. Other studies should include biodistribution studies (assessing if the GT product delivers to appropriate target and non-target tissues) and toxicology studies (assessing if this exposure is toxic).

3. Considerations for clinical trials.

The FDA provides recommendations regarding how to select the study population for clinical trials, how to appropriately and effectively design these studies, how to choose an appropriate GT product dose, and which endpoints are pertinent to measure success of these new therapies. Additionally, the FDA highlights suggestions to ensure that patients are safe during these clinical trials and emphasizes the need to document patient experience data.

This document was released along with five other guidance documents, such as Human Gene Therapy for Retinal Disorders, help stakeholders in developing new therapeutics using GT product technology.

Related News

- Gene Therapy in U.S. Is On Track for Approval as Early as Next Year
- MIT Technology Review – The first gene therapy for an inherited disease in the U.S. is closer to reality than ever before.
Rare Diseases: FDA Awards Grants for 21 Clinical, Natural History Studies [12]

Regulatory Affairs Professionals Society [13] – The US Food and Drug Administration (FDA) on Friday awarded $32 million in research grants to fund 15 clinical studies and six natural history studies for rare diseases.

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FDA awards 21 grants to stimulate product development for rare diseases [14]

FDA [15] – The U.S. Food and Drug Administration today announced that it has awarded 21 new clinical trial research grants totaling more than $23 million over the next four years to boost the development of products for patients with rare diseases.

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